

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of the claims in this application.

What is claimed is:

1. (Original) A modified human prolactin molecule comprising the following amino acid sequence:

| | | | | |
|--------------------|--------------------|--------------------|------------|--------------------|
| LPICPGGAAR | CQVTLRDLFD | RAVVLSHYIH | NLSSEMFSEF | <u>DKRYTHGRGF</u> |
| 10 | 20 | 30 | 40 | 50 |
| <u>ITKAINS</u> CHT | SSLATPEDKE | QAQQMNQKDF | LSLIVSILRS | WNE <u>PLYHLVT</u> |
| 60 | 70 | 80 | 90 | 100 |
| <u>EVGRMQE</u> APE | AILSKAVEIE | EQTKRLLEG | ELIVSQVHPE | TKENEIYPVW |
| 110 | 120 | 130 | 140 | 150 |
| SGLPSLQMA <u>D</u> | <u>EESRLS</u> AYYN | <u>LLH</u> CLRRDSH | KIDNYLKLLK | CRIIHNNNC |
| 160 | 170 | 180 | 190 | 199 |

wherein the prolactin molecule comprises at least one mutation in a region selected from i) at least one replacement, deletion, or insertion in amino acids 41-57, ii) at least one replacement, deletion, or insertion in amino acids 94-110, and iii) at least one deletion or insertion in amino acids 160-173, or replacement of an amino acid chosen from A, V, L, I, P, F, W, M, G, S, T, C, Y, N, Q, K, R, H in amino acids 160-173 with an amino acid chosen from D and E; ~~and wherein the at least one mutation is selected from deletions, replacements, and insertions.~~

2. (Original) The modified human prolactin molecule according to claim 1, wherein the prolactin molecule comprises at least one replacement mutation in region i), ii), and/or iii).
3. (Currently Amended) The modified human prolactin molecule according to claim 2, wherein at least one replacement mutation comprises replacing an amino acid ~~having a nonpolar or~~

~~hydrophobic side group~~, chosen from A, V, L, I, P, F, and M, with ~~a polar acidic~~ an amino acid that is ~~negatively charged at pH 6.0-7.0~~, chosen from D and E.

4. (Currently Amended) The modified human prolactin molecule according to claim 3, wherein at least one replacement mutation is chosen from F44E, F50E, I51E, A54E, I55E, L95E, L98E, V99E, V102E, L165E, L171E, and L172E.

5. (Currently Amended) The modified human prolactin molecule according to claim 2, wherein at least one replacement mutation comprises replacing an amino acid ~~having an uncharged polar side group~~, chosen from G, S, T, Y, N, and Q, with ~~a polar acidic~~ an amino acid that is ~~negatively charged at pH 6.0-7.0~~, chosen from D and E.

6. (Original) The modified human prolactin molecule according to claim 5, wherein at least one replacement mutation is chosen from T45E, T52E, N56E, S57E, Y96E, Y168E, and Y169E.

7. (Currently Amended) The modified human prolactin molecule according to claim 2, wherein at least one replacement mutation comprises replacing ~~a polar basic~~ an amino acid that is ~~positively charged at pH 6.0-7.0~~, chosen from K, R, and H, with ~~a polar acidic~~ an amino acid that is ~~negatively charged at pH 6.0-7.0~~, chosen from D and E.

8. (Original) The modified human prolactin molecule according to claim 7, wherein at least one replacement mutation is chosen from H46E, R48E, K53E, H97E, and H173E.

9. (Currently Amended) The modified human prolactin molecule according to claim 2, wherein at least one replacement mutation comprises replacing an amino acid ~~having an uncharged polar side group~~, chosen from G, S, T, Y, N, and Q, with an amino acid ~~having a nonpolar or hydrophobic side group~~, chosen from A, V, L, I, P, F, and M.

10. (Currently Amended) The modified human prolactin molecule according to claim 9, wherein at least one mutation is chosen from G47F and G49F.

11. (Currently Amended) The modified human prolactin molecule according to claim 2, wherein at least one replacement mutation comprises replacing ~~a polar basic~~ an amino acid that ~~is positively charged at pH 6.0-7.0~~, chosen from K, R, and H, with an amino acid ~~having a polar or hydrophobic side group~~, chosen from A, V, L, I, P, F, and M.
12. (Currently Amended) The modified human prolactin molecule according to claim 9 11, wherein at least one mutation is chosen from H46A, and R48A, ~~and H47F~~.
13. (Original) The modified human prolactin molecule according to claim 1, wherein the prolactin molecule comprises at least one deletion mutation in region i), ii), and/or iii).
14. (Original) The modified human prolactin molecule according to claim 13, wherein at least one deletion mutation comprises a single deletion of an amino acid chosen from amino acids 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, and 173.
15. (Original) The modified human prolactin molecule according to claim 14, wherein at least one deletion mutation comprises a deletion of F50.
16. (Original) The modified human prolactin molecule according to claim 13, wherein at least one deletion mutation comprises deletion of more than one amino acid chosen from amino acids 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, and 173.
17. (Original) The modified human prolactin molecule according to claim 16, wherein at least one deletion mutation comprises a deletion of amino acids^f chosen from 41-57, 94-110, 160-173,

41-49, 50-57, 41-42, 41-43, 41-44, 41-45, 41-46, 41-47, 41-48, 41-50, 41-51, 41-53, 41-54, 41-55, and 41-56.

18. (Original) The modified human prolactin molecule according to claim 1, wherein the prolactin molecule comprises at least one insertion mutation in region i), ii), and/or iii).

19. (Currently Amended) A modified human prolactin molecule that exhibits the following characteristics:

- 1) exhibits antagonist activity;
- 2) binds to prolactin receptor through site 1;
- 3) does not bind to prolactin receptor through site 2 or has ~~greatly~~ diminished binding through site 2; and
- 4) exhibits less than 1% of unmodified prolactin's agonist activity;

wherein the prolactin molecule comprises at least one mutation in a region selected from i) amino acids 41-57, ii) amino acids 94-110, and iii) amino acids 160-173; and wherein the at least one mutation is selected from deletions, replacements, and insertions.

20. (Original) The modified human prolactin molecule according to claim 19, wherein the prolactin molecule exhibits less than 0.9% of unmodified prolactin's agonist activity.

21. (Original) The modified human prolactin molecule according to claim 20, wherein the prolactin molecule exhibits less than 0.5% of unmodified prolactin's agonist activity.

22. (Original) A pharmaceutical composition comprising the modified human prolactin molecule according to claim 1 and at least one pharmaceutically acceptable excipient.

23. (Original) A method of treating a cancer comprising administering an effective therapeutic amount of the modified human prolactin molecule according to claim 1.

24. (Original) The method according to claim 23, wherein the cancer is breast cancer or leukemia.
25. (Original) The modified human prolactin molecule according to claim 1, with the proviso that the deletion is not of amino acids 41-52.
26. (Original) A method for reducing or suppressing lactation comprising administering an effective therapeutic amount of the modified human prolactin molecule according to claim 1.